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Antibiotic resistance of *Escherichia coli* from community-acquired urinary tract infections in relation to demographic and clinical data

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ABSTRACT

This prospective study determined the antibiotic susceptibility of 164 isolates of *Escherichia coli* from the urine of 164 patients (112 female, 52 male; mean age of 54.12 years) with community-acquired urinary tract infection (UTI). Half of the isolates were from uncomplicated UTI and half from complicated UTI (52 males and 34 females). Overall, 57.3% of isolates were resistant to ampicillin, 25% to co-trimoxazole, 20.1% to nalidixic acid, 14% to norfloxacin and ciprofloxacin, and 0% to fosfomycin and nitrofurantoin. Of the 82 isolates from complicated UTI, 16 (19.5%) were resistant to norfloxacin and ciprofloxacin, compared with seven (8.5%) from uncomplicated UTI (p 0.043). Isolates from patients aged >50 years were significantly more resistant than those from patients aged <50 years for nalidixic acid (p 0.007) and the fluoroquinolones tested (p 0.015). Resistance to fluoroquinolones was 25% (13/52) in males and 9% (10/112) in females (p 0.006). For patients with and without previous antimicrobial therapy, there was a significant difference only for resistance to nalidixic acid ($p < 0.001$) and the fluoroquinolones (p 0.011). There were adequate susceptibility rates to fosfomycin, nitrofurantoin and the fluoroquinolones for empirical use in the treatment of acute uncomplicated UTI. In order to interpret cumulative susceptibility data from the primary healthcare setting, it is necessary to take into account the type of UTI (uncomplicated vs. complicated), previous antimicrobial therapy, and the sex and age of each patient.

Keywords Antimicrobial resistance, *Escherichia coli*, community-acquired infection, quinolones, resistance, urinary tract infection

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INTRODUCTION

Acute uncomplicated cystitis is a significant problem in healthy non-pregnant women [1], with *c*.7 million community-acquired uncomplicated urinary tract infections (UTIs)/year in women in the USA [2]. In a recent prospective study in the USA, the incidence in young women was 0.5–0.7/person/year [3]. Among outpatients, *Escherichia coli* is the primary urinary tract pathogen, accounting for 75–90% of isolates from uncomplicated UTI [4]. In many cases, acute uncomplicated UTI in women is managed effectively and safely by empirical antibiotic therapy without the need for a urine culture. The rationale for this approach is based on the narrow and predictable spectrum of aetiological agents and their susceptibility patterns [5]. Laboratory testing is normally undertaken only when empirical therapy fails.

Knowledge of local susceptibility trends is an important consideration when selecting empirical therapy for UTI. The Infectious Diseases Society of America (IDSA) recommends that physicians obtain information on local resistance rates, and that ongoing surveillance be conducted to monitor changes in the susceptibility of uropathogens [6]. Numerous studies have demonstrated high and/or increasing antibiotic resistance levels in *E. coli* causing community-acquired UTI [7–20], but most in-vitro data come from laboratory-based surveys that often do not define the sex, age, clinical syndrome or other data of interest regarding the patients from whom the urine specimens were collected. In-vitro studies that specifically

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describe the antimicrobial susceptibilities of *E. coli* UTI isolates, and analyse the results in relation to demographic and clinical data, are limited.

In addition, because empirical therapy is being used widely, fewer UTIs are being cultured routinely. Thus, patients for whom culture results are available are likely to reflect a selection bias toward complications, recent treatment, recurrence of infection or suspected resistance. Thus, laboratory samples examined routinely may overestimate the true levels of antibiotic resistance in the community [21–24].

It is necessary to use new strategies to obtain more accurate data. In the emergency service of our hospital, nearly all UTIs treated are community-acquired, and a urine culture is performed routinely on suspicion of UTI. In addition, the Emergency Service sees a greater number of community-acquired complicated UTIs than are seen by a general practitioner, which permits a statistical comparison according to the type of UTI (complicated vs. uncomplicated). The present study assessed the antibiotic resistance of *E. coli* from community-acquired UTI in relation to demographic and clinical data, and the results obtained were compared with those obtained in 2002 for unselected isolates from the urine samples of outpatients.

MATERIALS AND METHODS

This prospective study included 164 isolates of *E. coli* from the urine of 164 patients with community-acquired UTI diagnosed in the Emergency Service of the Hospital de Móstoles (Madrid, Spain) between March 2002 and January 2003.

Susceptibility to ampicillin, gentamicin, fosfomycin, nitrofurantoin, cefazolin, nalidixic acid, norfloxacin, ciprofloxacin, and trimethoprim-sulphamethoxazole (co-trimoxazole) was determined using doubling dilutions in Mueller-Hinton broth in a commercially available microdilution system (Wider; Francisco Soria Melguizo SA, Madrid, Spain) [25]. The panels were inoculated with a standardised inoculum using a rehydrator-inoculator according to the guidelines provided by the manufacturer. The inoculum was prepared with the Prompt inoculation system (Francisco Soria Melguizo SA). After overnight incubation, the panels were introduced into the Wider system, which comprises a reader module and a data analysis module. Growth parameters in susceptibility testing wells were analysed in comparison with those in positive and negative control wells. The MIC of each antibiotic was defined as the lowest concentration with an absence of bacterial growth. For categorisation purposes, MICs were interpreted by NCCLS guidelines [26]. Intermediate and resistant results were grouped together for data analysis. Quality control was assured by including *E. coli* ATCC 25922 in every batch. All MIC determinations for this strain were within the ranges given by NCCLS for the antibiotics included in this study.

The clinical records of the 164 patients were reviewed to obtain demographic data (age and sex) and clinical data that enabled classification of the UTI as complicated or uncomplicated. Uncomplicated UTI refers to infection in a structurally and neurologically normal urinary tract. Complicated UTI refers to infection in a urinary tract with abnormalities. Cystitis describes the syndrome involving dysuria, frequency, urgency, and occasionally, suprapubic tenderness. Acute pyelonephritis describes the clinical syndrome characterised by flank pain or tenderness, or both, and fever, often associated with dysuria, urgency and frequency [27]. Antimicrobial therapy within the preceding 3 months was also recorded.

Differences in antibiotic resistance between different patient groups, together with calculation of the odds ratio (OR) and 95% confidence interval (CI), were analysed by the χ-square test or Fisher's exact test using SPSS software v.9.0 (SPSS Inc., Chicago, IL, USA). A two-tailed p value of ≤ 0.05 was considered significant. Data were obtained from the hospital laboratory concerning the sensitivity of *E. coli* isolates from outpatient urine samples during the year 2002.

RESULTS

The 164 *E. coli* urinary isolates were from 112 women and 52 males (mean age of 54.12 years; SD 21.15 years; range 17–91 years), with 82 (50%) from uncomplicated UTI (82 females; mean age, 46.34 years; SD 22.1 years) and 82 (50%) from complicated UTI (52 males and 34 females; mean age, 61.9 years; SD 17.02 years). Of the 82 patients with complicated UTI, five (6.1%) presented with kidney and urethral calculus, 13 (15.8%) with disorders of the urinary tract (11 anatomical and two functional), eight (9.8%) had urinary catheters, 14 (17.1%) suffered from diabetes mellitus, and 11 (13.4%) were immunosuppressed. Of the 82 women with uncomplicated UTI, 63 had acute cystitis (mean age, 50.14 years; SD 22.88 years) and 19 had acute pyelonephritis (mean age, 33.74 years; SD 13.18 years).

The antimicrobial resistance of the isolates is shown in Table 1. Of the 164 isolates, 23 (14%) were resistant to norfloxacin and ciprofloxacin. Of the 82 isolates from complicated UTI, 16 (19.5%) were resistant to norfloxacin and ciprofloxacin, compared with seven (8.5%) from uncomplicated UTI (OR 2.6; 95% CI 0.93–7.47; p 0.043). Antibiotic resistance to ampicillin, gentamicin, nitrofurantoin, fosfomycin, cefazolin, nalidixic acid and co-trimoxazole was also compared, but no statistically significant differences were observed. Similarly, no statistically significant differences were observed for any antibiotic when resistance in women with complicated UTI ($n = 30$) and uncomplicated UTI ($n = 82$) was compared.